Remarks/Arguments

Claims 32, 41, and 44-45 were rejected under 35 USC 103(a) over Vite et al in view of Nakajama et al. Applicants request reconsideration of this rejection for the reasons that follow.

This rejection is based on disclosure in Vite et al which suggests that a benefit may be derived by combining the disclosed epothilones, which act at the G2/M phase of the cell cycle, with another cytotoxic drug which acts at a different phase of the cell cycle. Nakajama et al is relied on as disclosing that a histone deacetylase inhibitor, FR901228, acts by blocking cell cycle transition at G1 and G2/M phases.

Vite et al sets forth a hypothesis which at best demonstrates what one of ordinary skill in the art would consider obvious to try. However, Applicants see no data or other information which would lead the skilled artisan to understand this disclosure to be any more than a suggestion of a promising field for further research.

Applicants assert that the rejection is improper based on the legal standards set forth in MPEP 2143(E) and the Federal Circuit's opinion in Bayer Schering Pharma AG v. Barr Laboratories, 575 F.3d 1341; 2009 U.S. App. LEXIS 17372; 91 U.S.P.Q.2D 1569 (Fed. Cir. 2009), and the case law cited therein, both of which provide guidance about the application an 'obvious to try' standard to reject claims in unpredictable arts, such as the treatment of cancer. It is clear that what is obvious according to the Examiner was merely to explore the general approach of combining epothilones with compounds that target a different phase of the cell cycle.

MPEP 2143(E) sets forth the Examiner's burden, according to the USPTO, to properly reject claims based on an 'obvious to try' standard:

> **E. . "Obvious To Try" - Choosing From a Finite Number of Identified, Predictable Solutions, With a Reasonable Expectation of Success**
> To reject a claim based on this rationale, Office personnel must resolve the Graham factual inquiries. Then, Office personnel must articulate the following:
> (1) a finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;
> (2) a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem;
> (3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and
> (4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

Applicants assert that the present rejection does not satisfy these requirements:

Applicants' position is further supported by the Federal Circuit's opinion in Bayer v. Barr:

> In KSR, the Supreme Court stated that an invention may be found obvious if it would have been obvious to a person having ordinary skill to try a course of conduct:
>
> > When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.
>
> 550 U.S. at 421. This approach is consistent with our methodology in *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988). See *Procter & Gamble Co. v Teva Pharms. USA, Inc.*, 566 F.3d 989, 996-97 (Fed. Cir. 2009); *In re Kubin*, 561 F.3d 1351, 1359, (Fed. Cir. 2009). *O'Farrell* observed that most inventions that are obvious were also obvious to try, but found two classes where that rule of thumb did not obtain.
>
> First, an invention would not have been obvious to try when the inventor would have had to try all possibilities in a field unreduced by direction of the prior art. When "what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful" an invention would not have been obvious. *O'Farrell*, 853 F.2d at 903. This is another way to express the KSR prong requiring the field of search to be among a "finite number of identified" solutions. 550 U.S. at 421; see also *Procter & Gamble*, 566 F.3d at 996; *Kubin*, 561 F.3d at 1359. It is also consistent with our interpretation that KSR requires the number of options to be "small or easily traversed." *Ortho-McNeil Pharm., Inc. v. Mylan Labs.*, Inc., 520 F.3d 1358, 1364 (Fed. Cir. 2008).
>
> Second, an invention is not obvious to try where vague prior art does not guide an inventor toward a particular solution. A finding of obviousness would not obtain where "what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *O'Farrell*, 853 F.2d at 903. This expresses the same idea as the KSR requirement that the identified solutions be "predictable." 550 U.S. at 421; see also *Procter & Gamble*, 566 F.3d at 996-97; *Kubin*, 561 F.3d at 1359-60.

Applicants assert that at best, the combined disclosure of the references suggest the general approach of combining therapeutic agents which block different phases of the cell cycle. However, it is clear that the presently claimed invention falls into the classes of invention where

what was 'obvious to try' is nevertheless patentable under the case law discussed in Bayer v. Barr. Therefore, Applicants assert that present rejection is improper and should be withdrawn.

Claims 32, 41, and 44-45 were rejected under 35 USC 103(a) over O'Reilly et al in view of Nakajama et al. Applicants request reconsideration of this rejection for the reasons that follow.

Applicants request the Examiner to reconsider this rejection in view of the discussion of the rejection over Vite et al above.

The Examiner cites In re Kerkhoven for the proposition that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art for the same purpose in order to make a third composition for the same purpose. Kerkhoven related to the preparation of a detergent by simultaneously spray drying two detergent slurries, whereas the prior art mixed all of the ingredients in a single slurry which was spray-dried. In finding the two slurry process obvious in the absence of unexpected results, Kerkhoven cites precedent to support the proposition that: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose."

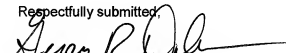
However, the situation decided in Kerkhoven yielded a predictable result. The present situation is clearly distinguished from Kerkhoven because of the unpredictability in treating cancer. At best, the combined disclosure of the references suggests an experiment. However, it provides no basis to select an epothilone and a histone deacetylase inhibitor. Additionally, the references provide only a theoretical basis to try the present combinations, which, as discussed above is not the proper basis for a rejection under 35 USC 103. Therefore, the present invention is patentable over the combined disclosure of the references.

Applicants have previously provided a copy of Funio et al., Mol. Cancer Ther., 2003;2:971-984, which provides data demonstrating that LAQ824, a histone deacetylase inhibitor, enhances apoptosis of breast cancer cells induced by epothilone B. Applicants assert that this demonstrates an unexpected benefit for the present combinations. The Examiner contends that the material does not appear to be commensurate in scope with the present claims which cover histone deacetylase inhibitors as a class. However, Applicants assert that the LAQ824 is representative of the histone deacetylase inhibitor class and provides an adequate basis to conclude that the entire class would show similar effects. Thus, the data is commensurate with the scope of the claims.

Applicants request withdrawal of the rejections under 35 USC 103(a) for the reasons discussed above.

Entry of this amendment and reconsideration and allowance of the claims is respectfully requested.

Respectfully submitted,



George Dohmann
Attorney for Applicant
Reg. No. 33,593

Novartis Pharmaceuticals Corporation
One Health Plaza, Bldg. 101
East Hanover, NJ 07936
(862) 778-7824

Date: May 27, 2009